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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,388	11/28/2000	Jin Hong	7682-051-999	8169

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PENNIE AND EDMONDS
1155 AVENUE OF THE AMERICAS
NEW YORK, NY 100362711

EXAMINER	
LUCAS, ZACHARIAH	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 09/24/2003

17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,388	HONG ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-16* is/are pending in the application.

4a) Of the above claim(s) *9, 13-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7, 8, 10-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some* c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3,4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, and the species wherein the virus is the respiratory syncytial virus (RSV), in Paper No. 16 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 7, 8, and 10-12 are pending and under consideration.

3. Claims 9, and 13-16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species/inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 16.

Information Disclosure Statement

4. The information disclosure statements (IDS) submitted on March 2, 2001, and March 22, 2001, are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner.

5. It is noted that the copy of reference BO (Sambrook et al.) of the March 22, 2001 IDS submitted by the applicant contains only a Table of Contents. The reference has therefore been considered only to the extent of the submitted material.

Priority

6. It is noted that this application has been amended to claim benefit of priority to the prior Application No. 08316,439, filed September 30, 1994. A reference to the prior application must be inserted as the first sentence of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e) or 120. See 37 CFR 1.78(a). **For benefit claims under 35 U.S.C. 120, the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications.** Also, the current status of all nonprovisional parent applications referenced should be included.

The application does not indicate the relationship of the present application to the priority document. Correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claim 12 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claim reads on a vaccine comprising a genetically manipulated virus of the paramyxoviridae family, wherein the genetic manipulation comprises any insertion, deletion, or substitution, and may also, optionally, comprise a heterologous sequence. The viruses of the paramyoviridae family are further

identified in the dependent claims as including the parainfluenza virus (PIV) and RSV. Thus, while the claims are broadly drawn to vaccines against any non-segmented, negative-stranded RNA virus, or to any paraxymovirus, the contents of the specification, and the dependant claims clearly indicate that the presently claimed invention is focused on vaccines against RSV.

In the specification, the Applicant has shown how to make attenuated RSV that may be able to raise an immunogenic response. Further, both the art and the Applicant agree that attenuated RSV is a good source of potential RSV vaccines. See e.g. Kahn, Curr Opin Pediatr 12(3): 257-62. However, the Applicant has not demonstrated that an RSV comprising any of the identified genetic modifications results in an effective RSV vaccine. Thus, while the Applicant has shown how to make genetically modified RSV in general, the Applicant has not provided any examples of, or demonstrated how to make, a modified RSV that is suitable as a vaccine.

In contrast to the Applicant's broad claims to vaccines against paramyxoviruses, including RSV, the application itself states that "[d]espite decades of research, no safe and effective RSV vaccine has been developed for the prevention of severe morbidity and mortality associated with RSV infection." App. page 4, lines 4-6. The application continues by generally discussing some of the failed approaches, which also highlight some of the problems associated with RSV vaccine development. These obstacles have been long recognized as obstacles to the development of an effective RSC vaccine (see e.g. Murphy et al., Virus Res 32: 13-36). These difficulties are still present, and still hinder the development of such a vaccine. An acknowledgement of such may be found in the June 2000 article by JS Kahn (supra, at 260) stating that the "prevention of RSV disease continues to be a challenge. See also, Crowe, Vaccine 20 (Supp 1): S32-S37 (teaching other obstacles from those in the Murphy article,

including difficulties specific to attenuated live vaccines). Thus, the art teaches that research in the development of an effective RSV vaccine is wrought with complexity, and that, given the complexity and numerous failures in the art, is highly unpredictable.

In view of the above, while the Applicant has shown how to make attenuated RSV that may be able to raise an immunogenic response, the Applicant has not demonstrated that any of the modified RSV disclosed in the application would be an effective RSV vaccine.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 7, 10, and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Gharpure et al., J Virol 3(4): 414-21 (of record in the March 2, 2001 IDS). These claims read on genetically manipulated RSV virus wherein the viral genome comprises a modification that is one of an insertion, substitution, or deletion. The reference teaches the induction of genetic changes in RSV genomes through exposure to chemical mutagens. Page 415. By doing so, and then isolating the mutagenized viruses. Thus, the reference teaches genetically manipulated RSV viruses, and therefore anticipates the identified claims.

11. Claims 7, 8, and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Park et al., PNAS 88: 5537-41 (of record in the March 2, 2001 IDS). These claims read on infectious genetically manipulated virus of the paramyxoviridae family, wherein the viral genome comprises a modification that is one of an insertion, substitution, or deletion. Park teaches a modified Sendai virus wherein the genomic coding regions were removed, and substituted with a heterologous gene. Page 5538. Thus, the reference anticipates the identified claims.

12. Claims 7, 10, and 11 are rejected under 35 U.S.C. 102(a) as being anticipated by Crowe et al., Vaccine 12(8): 691-99 (June 1994- of record in the IDS filed on March 2, 2001). These claims read on genetically manipulated RSV virus wherein the viral genome comprises a modification that is one of an insertion, substitution, or deletion. Crowe discloses a cold-passaged RSV designated as cp-RSV, and the introduction of additional mutations into the virus. See abstract. While the reference does not disclose what changes were made in the RSV genome in the making of the cp-RSV virus, the changes were later disclosed as a series of substitutions in the viral genome. See, U.S. patent 5,993,824, columns 4, and 77-78 (esp., table 36 in column 78). Thus, the cp-RSV mutation disclosed in the Crowe reference is a RSV comprising a substitution in its genome.

13. Claims 7, 8, 10, and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Collins et al., Virology 195: 252-56 (Collins I, July 1993- of record in the IDS filed on March 2, 2001) or by Collins et al., PNAS 88: 9663-67 (Collins II, also of record in the March 2001, IDS).

The claims read on the infectious RSV particles that have been genetically modified as described above, wherein the viral genome has been modified to encode a heterologous sequence. Each of these references teaches RSV particles wherein portions of the viral genome were deleted, and a heterologous chloramphenicol acetyl transferase (CAT) gene was inserted. Collins I, page 252; and Collins II, page 9663. These particles were then used to infect cells. Collins I, supra; Collins II, page 9665. Thus, the references anticipate the identified claims.

14. Claim 11 is rejected under 35 U.S.C. 102(a) as being anticipated by either of Conzelmann et al, J Virol. 68(2): 713-19, or Schnell et al., The EMBO Journal 13(18): 4195-4203 (September 15, 1994- of record in the March 22, 2001 IDS). The claim described genetically manipulated infections, non-segmented, negative-stranded RNA virus, the genome of which comprises a modification that is one of an insertion, substitution, or deletion. These references teach the making of recombinant rabies virus comprising, alternatively and cumulatively, deletions, and additions to the genome.

Conclusion

15. No claims are allowed.

16. The following prior art reference is considered pertinent to applicant's disclosure as describing the state of the art at the time of the applicant's filing. U.S. Patent 5,716,821, issued to Wertz et al.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner

James C. Housel
9/22/03

JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600